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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,006	10/25/2001	Bruce H. Morimoto	5412/1E887US2	4547

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	**PAPER NUMBER**
1615	1

DATE MAILED: 03/31/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/890,006	MORIMOTO ET AL.	
	Examiner	Art Unit	
	Gollamudi S Kishore, PhD	1615	

-- The MAILING DATE of this communicati n appears on the cov r sheet with the correspondenc address --

P ri d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

In view of applicant's letter dated 9-23-03, the previous office action is vacated. The following is the new action.

Claims included in the prosecution are 1-21.

Claim Rejections - 35 USC § 112

1. Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds wherein phosphocholine is directly linked to steroids, does not reasonably provide enablement for attachment through multitudes claimed linkers and multitudes of moieties defined in X. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d, 1400 (Fed.Cir.1988). Among these factors are: (1) the nature of the invention; 2) the state of the prior art; 3) the relative skill of those in the art; 4) the predictability or unpredictability of the art; 5) the breadth of the claims; 6) the amount of direction or guidance presented; 7) the presence or absence of working examples; and 8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

1) The nature of the invention: the invention concerns with compounds wherein a phosphocholine is attached to a therapeutic compound through various linker units.

2) The state of the prior art: the state of the prior art is very high in terms of attaching therapeutic drugs to phospholipids; however, it is unclear however, whether one could prepare compounds through multitudes of linkers and X moieties as recited only in claims 1-9.

3) The relative skill of those in the art: the skill of one of ordinary skill in the art is very high (Ph.D level technology). It should be pointed out preparation of compounds, if they can be prepared takes years of bench work.

4) The predictability or unpredictability in the art: it is unclear whether multitudes of compounds can be prepared at all and if they can be prepared whether they would retain the drug efficacy since it depends on the efficient release from various linker units.

5). The breadth of the claims. The breadth of the claims is very broad in terms of the linker units and the X moieties

6) The amount of direction of guidance provided: instant specification provides no guidance at all in terms of how various linkers and X moieties are attached to various drugs claimed. In fact, the specification does not even recite these linkers and X moieties and the drugs claimed.

7) The presence or absence of working examples: the only working example provided is the attachment of specific steroid with phosphocholine by direct linkage and not through linkers and X moiety.

8) The quantity of experimentation necessary: since instant specification does not provide adequate guidance, it is difficult for one of ordinary skill in the art to choose the proper linker and X moiety and the drug without undue experimentation. Broad claims must have broad basis of support in the specification; in the absence of such support, claims must be limited to drugs attached directly to the phosphocholine.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

2. Claims 12, 14, 15, 18 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

'related anesthetic or sedative compounds' in the Markush expression renders claim 12 indefinite. It is not a positive recitation. Specific compounds should be recited. It is also unclear as to what "Propofol" represents. It is spelled with capital letter P in this claims and not so in claim 20. Instant specification does not state what this compound is.

Claim 1 is a compound claim; claim 14 recites further comprising and is dependent claim. The examiner suggests "a composition comprising compound of claim 1 and one or more ingredients ------" in claim 14. The distinction between carriers and excipients is unclear.

Claim 15 is incomplete; there is a question mark next to ocular.

Claim 18 recites, "increasing the aqueous solubility of a pharmaceutically active agent". What is conjugated to the active agent is a lipophilic phospholipid; that means the complex of a poorly water-soluble compound is more lipophilic than the active compound itself. Then how can one increase the aqueous solubility? Clarification is requested.

What is being conveyed by 'flavor as called for by accepted pharmaceutical practice' in claim 21?

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-11, 13-15, 18-19 and 21are rejected under 35 U.S.C. 102(a) or (b) as being anticipated by Chasalow (5,830,432) of record.

Chasalow discloses compounds wherein a drug is attached to phosphocholine through an NH2 group (X), which in turn is attached to a substituted alkenyl moiety or alkyl (linker) and methods of increasing the aqueous solubility of bioactive agent by conjugating them to phosphocholine moieties. According to Chasalow, any active agent

could be used and those include steroids and aspirin (note the abstract, col. 2, line 25 through col. 4, line 65; examples and claims).

It would appear that many of the compounds do not appear to have support in the PCT application and support in the provisional application is also unclear. These rejections will be reconsidered, once the support in the priority papers is determined.

5. Claims 1-11, 13-15, 18-19 and 21are rejected under 35 U.S.C. 102(a) or (b) as being anticipated by Ansell (5,534,499).

Ansell discloses taxol attached to phosphocholine through claimed linker and X moieties (note the abstract, col. 1, line 21 through col. 2, line 44; columns 3-9, examples and claims).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 12, 16-17 and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chasalow (5,830, 432)

The teachings of each of Chasalow have been discussed above. What are lacking in Chasalow are the teachings of the attachment of instant drugs. However, in view of reference's suggestion that the method is applicable to any active agent and from the guidance provided by the reference, it would have been obvious to one of

ordinary skill in the art to use any active agent with a reasonable expectation of success.

8. Claims 12, 13, 16-17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ansell (5,534,499) cited above.

The teachings of Ansell have been discussed above. What are lacking in Ansell are the teachings of instant drugs. However, in view of reference's suggestion that the method is applicable to any active agent and from the guidance provided by the reference, it would have been obvious to one of ordinary skill in the art to use any active agent with a reasonable expectation of success.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1234.

Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK